IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	SAKANE et al.	Examiner:	Foreman, Jonathan
Serial No.:	10/527417	Group Art Unit:	3736
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Title:	MEDICAL GUIDE WIRE AND PROCESS FOR PRODUCTION THEREOF		

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DECLARATION UNDER 37 C.F.R. §1.132

Dear Sir:

I Hiroshi YAMADA, a citizen of and residing in Japan, hereby declare as follows:

I am a citizen of Japan, born in Aichi prefecture, Japan on January 16, 1975. I reside at 1-7-6, Aoyama, Otsu-city, Shiga prefecture, Japan. I completed my master's course in the Graduate School of Engineering, Applied Chemistry at Kansai University on March 31, 2000, joined I.S.T (Industrial Summit Technology) in April, 2000 mainly in charge of developing the molding technology of polymeric chemistry such as fluororesins and polyimide resins, and have been in charge of developing medical guide wires since around June 3, 2002. I am one of the inventors of the present invention in Patent Application No. 10/527,417. I am familiar with the efforts to develop and commercialize the product of the present invention and with the market for and history of medical guide wires.

1. Background

At early stages of the medical guide wire field, in general, the catheter has been used for inspecting a human body (ANNEX 1). However, presently, the catheter also is being used for a catheter surgery (catheter treatment) (ANNEX 2). The catheter surgery is a method in which a

thin tube (catheter) is inserted into a blood vessel through a puncture in the skin several milliliters in diameter at the time of performing a treatment or surgery for diseases in organs such as the heart, the blood vessels, the brain, the liver, the digestive organs and the urinary organs. This method is advantageous in that it imposes a much smaller burden on the patient, as compared with a conventional method in which a large incision is made on the skin tissue using a scalpel under a general anesthesia (ANNEX 3). The medical guide wire is used with the catheter in performing the catheter surgery (ANNEX 2).

There have been two main methods for increasing the slidability of the medical guide wire to make it more useful in surgical and therapeutic procedures.

One method is called "hydrophilic coating", which increases slidability by coating a hydrophilic gel on an object and allowing the hydrophilic gel to contain water. When the hydrophilic gel absorbs water in blood, a water film is formed with respect to the object, thereby realizing greater slidability. This method is used for an inspection guide wire. However, when the guide wire having the hydrophilic coating is used in the body, the blood present around the guide wire dries due to the manipulation by the doctor during treatment. Once the surface is dried, the hydrophilic coating loses its slidability. Therefore, hydrophilic coating cannot be used on therapeutic guide wires.

Another method is to coat a surface of an object with fluororesin. A medical guide wire obtained by the second method is mainly used as a surgical or therapeutic guide wire. Almost all of the guide wire makers have chosen this latter method of coating the guide wire surface with the fluororesin coating to increase the slidability of the medical guide wire.

The guide wire of the present invention has low frictional force with respect to a catheter tube and has high slidability, thereby greatly contributing to the development of the catheter surgery (intervention).

We have long experience and have own technical strength in the coating technology of the fluororesin. US Patent 4781972 B, US Patent 4707387 B, US Patent 5582886 B and the like are given as examples of effects of our inventions, which are now used in the world market.

With such a background, as a development course of the medical guide wire, we set an object to develop a guide wire that realizes slidability at least about twice as high as that of the conventional fluororesin-coated guide wire.

In the process of studies, we blended fluororesins having different melting points and coated it on a glass plate. From the microscopic observation, we found that the fluororesin having a low melting point was perfectly melted when baked and formed as a coating film, whereas the fluororesin having a high melting point partially was not melted, solidified in a state like a foreign substance and remained on the surface of the fluororesin coating. We further found that the slidability of this coated surface became extremely high. However, this phenomenon was unable to be observed visually, and at first we were even uncertain why the slidability of this tested substance was increased.

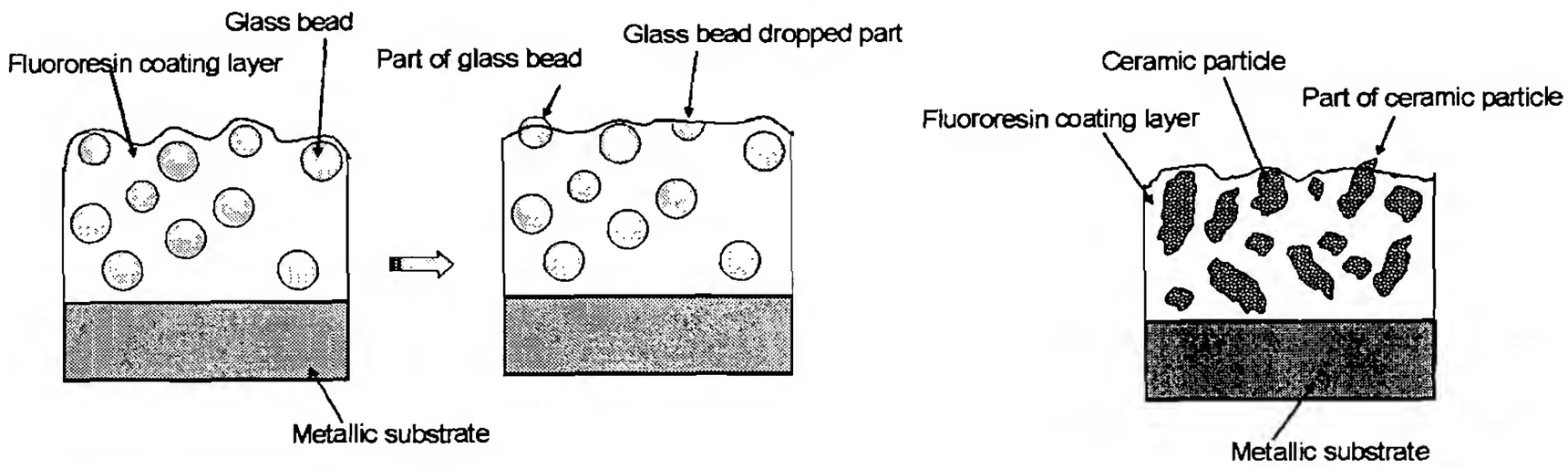
After continuing studies and experiments for developing this experimental result on the surface of the 0.35 mm diameter wire with the fluororesin coating thickness of 5 μm, observing the surface of the wire using an electron microscope and a super depth-shape measuring microscope capable of observing the height and shape of the solidified fluororesin, and clarifying the relationship between slidability and data on the height and shape of the solidified, protrusion-shaped fluororesin, the density of the developed protrusion-shaped matter and the like, we were able to accomplish the present invention.

In the process of developing the present invention, likewise the fluororesin coating on cookware such as a frying pan (approximate to US 6,291,054 (Thomas et al.) indicated by the Examiner), available under the E.I. du Pont de Nemours trademark "SilverStone", we also had tried the method several times in the experimental stage in which ceramics for imparting wear resistance is mixed into a fluororesin solution so as to coat the wire thickly in multi-layer, and recessions and protrusions are formed on the surface of the fluororesin coating, for the purpose of increasing the slidability with a contact object.

In other words, ceramics and glass beads were mixed in the fluororesin solution and applied to the wire. Although preferable results were obtained in the first and second friction tests, bodies of the ceramics and glass beads were easily exposed from the surface of the fluororesin coating after the friction test was repeated several times, since the fluororesin coating had only the thickness of 5 μm. Consequently, these bodies scratched a material in contact therewith, which adversely reduced the slidability.

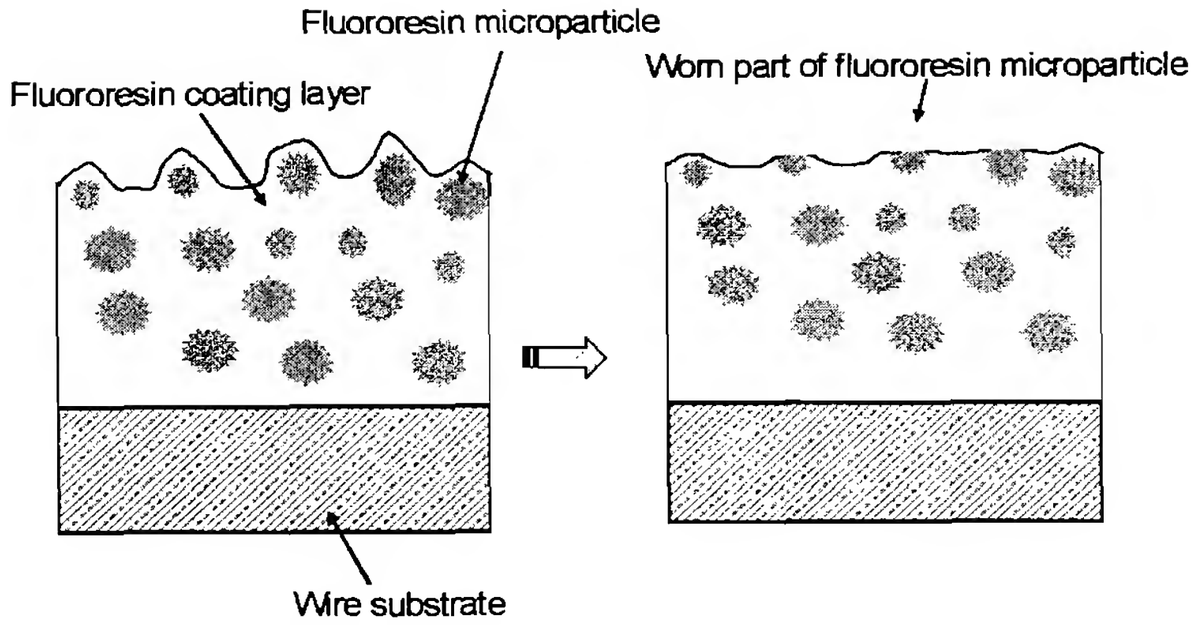
In actual surgical conditions, the guide wire comes into contact with and rubs with the internal surface of the catheter at a frequency of about 50 to 100 times when used. Under such severe conditions of use during surgery, as shown conceptually below in FIG. 1, not only can ceramics and glass beads scratch and damage the material in contact therewith, but also they themselves come off and drop from the fluororesin. Needless to say, this is unacceptable for a product to be used in surgery.

[FIG. 1]



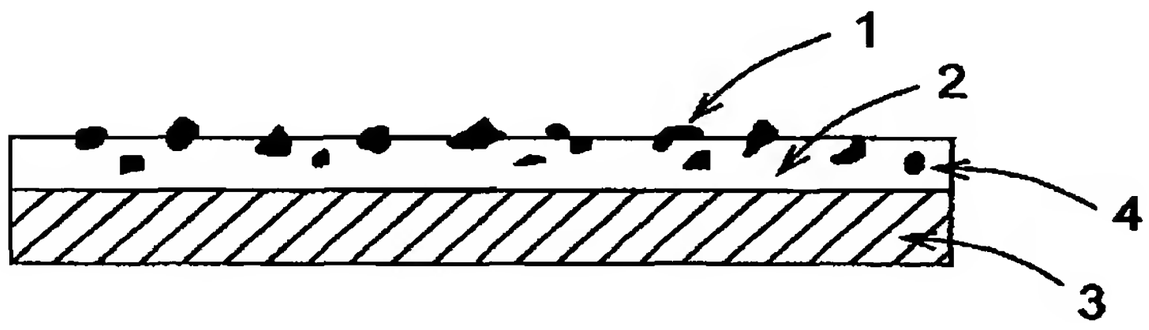
Further, the medical guide wire of the present invention is "a medical guide wire in which at least a fluororesin coating layer is formed on a surface of a metal wire, wherein the metal wire has a uniform thickness or a tapered tip; wherein a particulate matter of fluororesin is present in the fluororesin coating layer, the fluororesin coating layer and the particulate matter of fluororesin are baked by heating at at least a melting point of the fluororesin coating layer, and the fluororesin coating layer and the particulate matter of fluororesin are compatible and melt into a single unit; and wherein the fluororesin coating layer is an outermost layer that covers the particulate matter, and at least some of the particulate matter is formed in surface protrusion-shaped smooth projections", and the thickness of the fluororesin coating is thin (1 μm or more, 50 μm or less). Such a thin coating might be expected to be worn out by the severe conditions of use during surgery. However, as shown in FIG. 2, even if the coating is worn out, the inside is also fluororesin; besides, since the fluororesin coating layer and the fluororesin microparticles respectively are melted by baking to be formed into a single unit, no fluororesin particles drop. Further, the medical guide wire of the present invention is inert chemically, which maintains slidability and provides safety in use.

[FIG. 2]



Meanwhile, as for the invention of US 2,002,172,829 A1(Mori), as shown in FIG. 3, the fluorine-containing polymer 1 and the non-fluorine-coating polymer 2 (coating layer 4) are not melted by baking to be formed into a single unit, whereby the fluorine-containing polymers 1 drop from the surface of the coating layer easily.

[FIG. 3]



The present invention adopts a blend of a water-dispersible fluororesin suspension (fluororesin dispersion) and a fluororesin powder as a coating material of the wire.

The fluororesin coating solution used in the present invention is a solution in which a fluororesin powder is blended into a fluororesin dispersion. The fluororesin dispersion is obtained by emulsion polymerization in such a manner that raw fluororesin particles are dispersed in water by a surfactant. Further, examples of the fluororesin power include a fine powder that is obtained by coagulating and separating particles obtained by the emulsion polymerization from the dispersion, a powder that is obtained by pulverizing the baked

fluororesin, and the like. Since these powders were hardly blended into water, and separated and precipitated in the water, the blend gave us many challenges. Consequently, we found a method for avoiding the separation and precipitation of the fluororesin powder even after being left for a long time, by adjusting the additive amount of the fluororesin powder, the timing of the addition, the agitation speed, the agitation intensity, and by selecting the particle size.

At the same time, a long-term effort was required to develop a method of applying the powder and the dispersion in the fluororesin coating solution simultaneously and uniformly in the thickness of 5 μm, to the surface of the 0.35 mm diameter wire. We established a plurality of relative conditions, such as the viscosity of the fluororesin coating solution, the surface tension, the temperature of the solution when applied to the wire, the moisture immediately after the application, and the like. Thereby, it also becomes possible to apply the fluororesin powder in the coating solution to the surface of the wire in the uniform ratio.

The next development factor is to develop the drying and the baking of the wire coated with the fluororesin coating solution. Baking the fluororesin at a high temperature of 327°C or more allows the formation of the strong fluororesin coating on the wire surface. However, since fluororesin powders having not so much differences in the melting point were blended in the fluororesin dispersion, the fluororesin powders exposed for a little long time under high temperature exceeding the melting point of the fluororesin also were melted perfectly, whereby the shapes of the powders were deformed and the required protrusion shapes were not obtained. Further, when the baking time was short, the powers remained without being baked, which results in decline in the slidability and the drop of the powders.

From these results, in order to form the protrusion-shaped projections, it was required to find conditions of the baking temperature and the baking time. From a number of experimental results, we established a condition that enables the formation of protrusion-shaped projections at a baking temperature of 380 to 450°C exceeding the melting point of the fluororesin for 20 to 60 seconds, using a heater capable of generating infrared light of 0.9 to 5.6 μm.

Accordingly, the guide wire of the present invention has low frictional force with respect to a catheter tube and has substantially improved slidability over the prior art devices.

2. Commercial Success

Our developed medical guide wire is "a medical guide wire in which at least a fluororesin coating layer is formed on a surface of a metal wire, wherein the metal wire has a uniform thickness or a tapered tip; wherein a particulate matter of fluororesin is present in the fluororesin coating layer, the fluororesin coating layer and the particulate matter of fluororesin are baked by heating at at least a melting point of the fluororesin coating layer, and the fluororesin coating layer and the particulate matter of fluororesin are compatible and melt into a single unit; and wherein the fluororesin coating layer is an outermost layer that covers the particulate matter, and at least some of the particulate matter is formed in surface protrusion-shaped smooth projections", and the greatest characteristic thereof is its high slidability (low friction property). Terumo Corporation, a sale destination of our guide wire, started to bring our developed medical guide wires having high slidability to the market in 2004 (ANNEX 4).

We visited hospitals in Japan (Shiga Medical Center for Adults, Toyohashi Heart Centre, Kurashiki Central Hospital, etc.) for conducting our own discussions with doctors about the slidability of our medical guide wire. The doctors have stated that "the increased slidability has surely improved the operability of the guide wire, and consequently, the success rate of surgery is increased." In view of this, we understand the importance of allowing the medical guide wire to have high slidability as its principal characteristic that has led to the commercial success of the present invention.

The guide wire of the present invention accomplished by overcoming various technical challenges has started to be adopted by Terumo Corporation, Japan since 2004 (ANNEX 4), has been sold to medical institutions, and actually has acquired commercial success. Despite the late start in the market, we have increased the market share of our guide wires as follows: 11% in 2005; 20% in 2006; 26% in 2007. In 2007, we overtook a 25% share of Abbott, winning the second market share in Japan, and were close to a 33% share of Asahi Intecc Co., Ltd., Japan. Then, in the midterm financial report of Terumo Corporation in the fiscal year ending March 2008, it was reported that our medical guide wire won a top share in Japan (according to the documents for the financial result briefings of Terumo Corporation in 2007 and 2008).

Presently, our guide wires stay ahead of domestic competitors, winning a top share in Japan. It is reported in the newspaper that they are also exported to countries throughout the world.

The sales volume of the medical guide wire of the present invention by Thermo Corporation is 350 to 400 thousands guide wires annually as of January, 2010, with more than 1.5 million guide wire sales in total in the past six years.

The commercial success of the medical guide wire of the present invention has been due to the following excellent characteristics.

(1) Since the surface is coated by the fluororesin layer and formed with the protrusion-shaped smooth projections, it exhibits unprecedented slidability. The measurement results of the slidability (frictional resistance) of the medical guide wire of the present invention were: 2.0 g in Working Example 1; and 1.8 g in Working Example 2, which were less than half of the frictional resistance of the general fluororesin coating product, i.e., 4.5 g (Comparative Example 1). Further, the slidability of the guide wire only coated with fluororesin sold by Boston Scientific Corporation U.S. (trade name "CHOICE™") was measured using the same method as that of the present application, which resulted in 3.5 g. This proves that the slidability of the guide wire of the present invention is significantly high as compared with the competitor's product. Incidentally, the outer diameters of the guide wire of the present application and "CHOICE™" are the same but harnesses thereof are different. Therefore, based on the data on the hardness and slidability of the wire, the above result was calculated by a formula that allows "CHOICE™" to be compared under the same condition as Working Examples.

These results are summarized in the table below.

Experimental number	Working Example 1	Working Example 2	Comparative Example 1 (only fluororesin)	Competitor's Product
Frictional Resistance (g)	2.0	1.8	4.5	3.5

(2) Further, since the medical guide wire of the present invention has a low frictional resistance, it has excellent operability for a doctor during an operation, thereby shortening an operation time. The shortened operation time makes it possible to reduce the time while a patient must endure a pain and also reduce medical costs.

(3) Moreover, we believe that high evaluation in the market allows us to sell over 1.5 million guide wires in the past six years and to produce 350 to 400 thousands guide wires continually every year. In other words, the guide wire of the present invention is "a medical guide wire in which at least a fluororesin coating layer is formed on a surface of a metal wire, wherein the metal wire has a uniform thickness or a tapered tip; wherein a particulate matter of fluororesin is present in the fluororesin coating layer, the fluororesin coating layer and the particulate matter of fluororesin are baked by heating at at least a melting point of the fluororesin coating layer, and the fluororesin coating layer and the particulate matter of fluororesin are compatible and melt into a single unit; and wherein the fluororesin coating layer is an outermost layer that covers the particulate matter, and at least some of the particulate matter is formed in surface protrusion-shaped smooth projections". Furthermore, since only the fluororesin that is generally inert to the human body is used as a material to coat the wire, and the fluororesin coating layer and the fluororesin particles are formed into a single unit, our guide wire causes no drop of particles even under the severe operation during treatment and can be used without anxiety. We believe that these are the reasons why our guide wire is evaluated as the product offering high safety with respect to the human body and high slidability.

(4) The medical guide wire of the present invention is used not only in Japan but also exported to the U.S.A, Europe and other countries.

3. Conclusion

As described above, the medical guide wire of the present invention has a low friction force to a catheter tubes and has high slidability, and therefore, we believe that our guide wire is greatly conducive to the development of the catheter surgery (intervention) and contributes greatly to the medical industry.

4. ANNEXES

ANNEX 1: Internet, Wikipedia, Catheter (with English translation)

ANNEX 2: Internet, Catheter Surgery (with English translation)

ANNEX 3: Internet, Japan Cardiovascular Intervention (with English translation)

ANNEX 4: Internet, Brochure of Terumo Corporation

I, the undersigned declarant, declare under the penalty of perjury that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and with the knowledge that willful false statements may jeopardize the validity of the above patent application or any patent issuing thereon.

Signed this September 29, 2010, at Shiga, JAPAN

Hiroshi Yamada

Hiroshi YAMADA